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THE BRITISH JOURNAL OF DERMATOLOGY

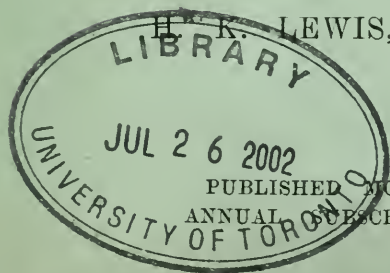
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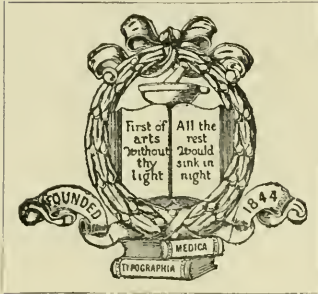
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THE BRITISH JOURNAL OF DERMATOLOGY.

DECEMBER, 1908.

THE EPITHELIUM OF THE BUCCAL MUCOSA.

By W. THOROLD QUAIFF, M.B. CH.M.(SYD.), D.T.M.&H.(CAMP.).

THE structure and evolution of the epidermis is now comparatively well understood, and the process of cornification has been worked out.

The same cannot be said of mucous membranes, which have received scanty consideration in comparison.

The chief object in making this contribution is the possibility by so doing of clearing up the question whether the buccal epithelium possesses a layer of cells containing keratin, it being frequently stated, especially in connection with leucoplakia of the tongue, that horny thickenings do occur.

By buccal mucosa, in this paper, is meant the epithelium of the mouth cavity, including that of the tongue, of the cheeks, and of the moist inner surface of the lips—the dry, red portion of the lips being epidermal. The epithelium of the lower portion of the vagina shows structure identical with that of the buccal mucosa; the labia minora, however, usually possess an epidermal covering.

The buccal mucosa is a stratified epithelium, consisting, as does the epidermis, of a basal layer of proliferating cells, the daughter-cells of which differentiate as they approach the surface to form a protective layer and are finally cast off. But the details of the differentiation and the nature of the protective cell differ from those of the epidermis and the epidermal horn cell. The epithelium is much softer than the epidermis, and it is constantly moist. (See Figs. 1 and 2.)

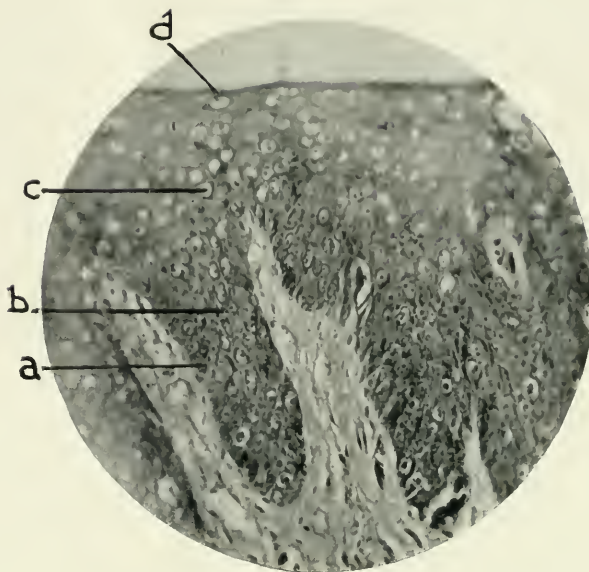
The differentiation of the daughter cell.—The proliferating cells of the basal layer and at first the daughter-cells closely resemble the corresponding cells of the epidermis. When removed from the basal layer by some four or five cells the cell is considerably larger than the mother-cell, and shows an oval, loose-meshed nucleus and granular protoplasm; no perinuclear space is found. The cells are many-sided from mutual pressure. Distinct intercellular lymphatic spaces are present, but are very narrow, and are crossed by “prickles” as in the epidermis. The cell now becomes larger and more fusiform, with the long axis parallel with the surface, and as it approaches the surface becomes more globular but with fusiform extremities. The nucleus becomes larger and the chromatin looser, more “vesicular.” Around the nucleus appears a non-staining space which becomes greater as the cell enlarges towards the surface. The periphery of the cell shows a narrow margin of protoplasm or merely a deeply staining line. Often there is a slender network between the nucleus and the periphery, but this is not always present. In some cells the peripheral line is indented at the junction of one of the fibrils, suggesting intra-cellular pressure. Intercellular lymphatic spaces are very narrow; the prickles between the cells are well-marked if suitable stains be used. The most superficial cells show these points most plainly, but between them no intercellular spaces can be seen.

Of these cells there are many layers.

Almost abruptly towards the surface the cells change in character. The nucleus become smaller, denser, and rounded, and the cell fusiform and compressed, showing little or no clear perinuclear space and the final stage is reached. Here the cell is flattened, fusiform in vertical section, with a flattened nucleus and no appreciable contents but the nucleus. Normally these protective cells form a thin layer on the surface, three to four cells thick.

The papillæ in some situations resemble the papillæ of the epidermis, with narrow interpapillary processes, but more often these are broad (Fig. 2) and rounded and with narrow papillæ between them, and then the differentiation over the papillæ is rapid from mother-cell to the surface, showing few of the large clear cells, but in the interpapillary process these cells are present in large numbers and give a very characteristic appearance to this epithelium. The kerato-hyalin and eleidin of the epidermis are not present.

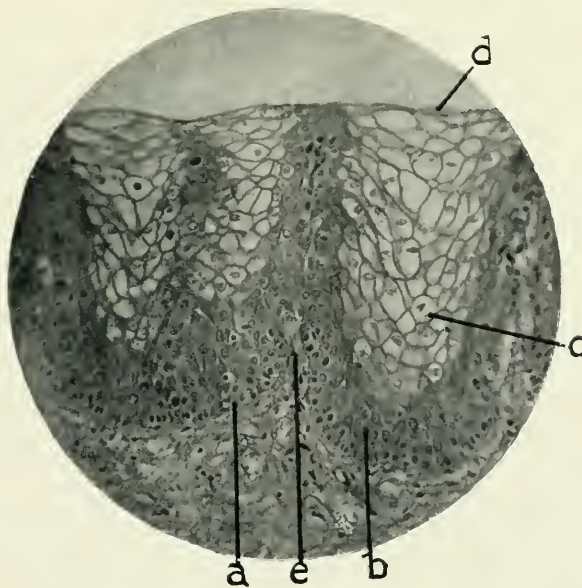
FIG. 1.



Section of normal mucosa from the inner surface of the lower lip.

a. Basal proliferating layer. *b.* Daughter-cells hardly yet differentiated. *c.* Daughter-cells showing change into cells with small nucleus and large perinuclear space. *d.* Superficial layer of cells.

FIG. 2



Section of normal mucosa from the inner surface of the lower lip.

a. Basal proliferating layer. *b.* Daughter-cells hardly yet differentiated. *c.* Daughter-cells showing change into cells with small nucleus and large perinuclear space. *d.* Superficial layer of cells. *e.* Papilla.

The junction of the mucous epithelium with the epidermis.—This is found in the red portion of the lips at the line where the dry, finely fissured portion joins the smooth, moist epithelium. The dry, finely fissured portion shows the normal epidermal structure. In the case of the vulval mucosa I have not found the line of junction to be quite constant; in some cases the mucosa ended at the line where the vagina becomes continuous with the labia minora, these being covered entirely with epidermis, but in other cases the junction was at the free border of the labia minora, the outer aspect being covered by epidermis and the inner by mucous epithelium. In any position, either lip or vulva, the change is abrupt.

The superficial protective cells.—The thin layer on the surface corresponding with the horny layer of the epidermis consists of nucleated cells, smaller than epidermal horn-cells. In vertical section they are fusiform, containing a narrow nucleus.

To obtain separated individual cells, a piece of fresh mucous membrane from the inner surface of the cheek was macerated in peroxide of hydrogen, to which some 5 per cent. phenol was added to prevent the growth of bacteria. After twenty-four hours the superficial cells were gently scraped off and films were made and were stained by Rausch's method. These films show irregular, many-sided cells, invariably nucleated, the nucleus oval, dense, and about one third of the diameter of the cell. No keratin prickles are present, but merely a deeply staining blue nucleus and faint pink or blue, clear protoplasm. In no instance were keratin prickles or anything suggesting a keratin framework to be seen. Some films were then digested in a solution of pepsin ($\frac{1}{2}$ per cent.) in hydrochloric acid (1 per cent.) for twelve, twenty-four, and forty-eight hours. These films stained by Rausch's method showed that the majority of the cells dissolved completely, a few were represented by finely-granular *débris*, and in a few instances the nuclei were left undissolved. No keratin prickles could be seen.

Pieces of fresh tissue were then digested in the acid pepsin solution:

- (1) Epidermis, as a control.
- (2) Mucous membrane from the lip and from the vulva, the latter including a part of the vaginal wall and a part of one of the labia minora.

After twenty-four hours the tissues were almost wholly dissolved and crumbled away as one attempted to lift them, but a jelly-like film on the surface of the epidermis was obtained, from which films were made and were stained by Rausch's method, showing the usual epidermal horn-cells with keratin prickles. Similar films were made from the surface of the piece of vulval tissue, but only from the

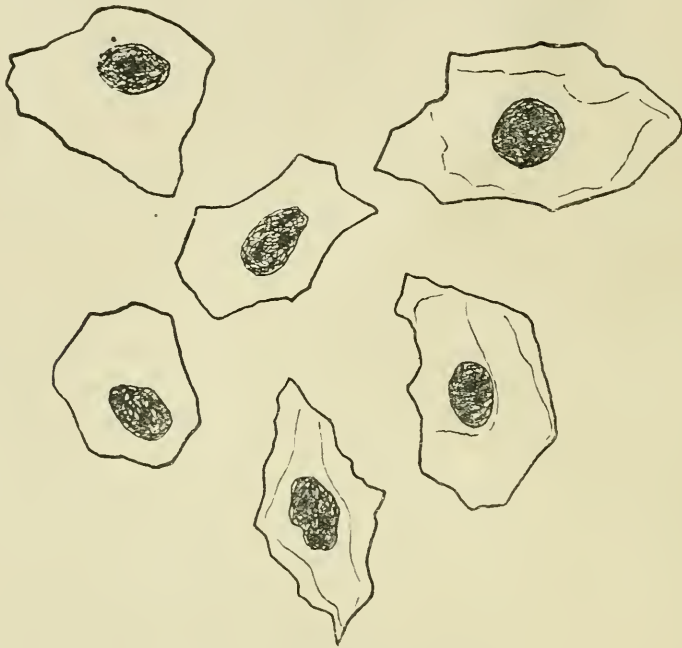


FIG. 3.—Superficial cells.

labial or epidermal part of this, the vaginal part being completely dissolved. The tissue from the lip was also completely dissolved. This would show that no substance resisting the digesting fluid is present in mucous membranes.

Pieces of fresh tissue were then embedded in celloidin, lip mucosa, and epidermis, and thick sections were cut (20μ) and were treated with fuming nitric acid for two hours. The epidermal sections showed the horny layer as a meshwork of yellow-stained keratin, all other constituents being dissolved. But the sections of mucous membrane were completely dissolved.

Pathological thickening of the buccal mucous membrane.—Films were

made from scrapings from the patches of thickened mucosa from two cases: (1) A case of extensive leucoplakia buccalis affecting the tongue and the inner aspect of the cheeks of two years' duration, and now slowly resolving. (2) A case of Lichen planus showing a few patches on the tongue and the cheeks.

The films were stained by Rausch's method and showed epithelial cells containing and surrounded by large numbers of bacteria, which made it difficult to decide whether prickles were present or not. But in a proportion of the cells quite definite prickles were seen staining a reddish tint, and then even amongst the blue-stained bacteria they could be distinguished in the majority of these cells from both cases. The cells were mainly larger than those of normal mucosa, and from a large proportion of them the nucleus had disappeared. They approach, therefore, more closely to the type of the cell found in films from the epidermis.

Other films from these cases were digested in the acid pepsin solution. Here the cells were mainly represented by groups of bacteria, after staining by Rausch's method, showing the original shape of the cell. In none could prickles be distinguished, showing that the prickles of the cells are not keratin.

SUMMARY.

(1) The buccal mucosa resembles in its general structure the epidermis, in possessing a proliferating basal layer of cells, the daughter-cells of which differentiate to form finally a layer of protective cells.

(2) The daughter-cell appears in the later stages of its differentiation as a large cell with a small nucleus, scanty peripheral protoplasm, and relatively a large, clear perinuclear space.

(3) No kerato-hyalin nor eleidin are present.

(4) In the deeper portion the intercellular lymphatic spaces are well marked and are crossed by numerous distinct "prickles."

(5) The superficial protective layer is composed normally of nucleated cells smaller than epidermal horn-cells, and these cells do not possess keratin "prickles" nor any form of keratin.

(6) At the junction of the epidermis and the mucosa the change from one to the other is usually very abrupt.

(7) In certain pathological conditions of thickening of the mucosa the cells have advanced farther in their differentiation, resembling the epidermal horn-cell more closely in being larger and having no nucleus and possessing definite "prickles," which, however, are not of the nature of keratin.

In conclusion, I must express my gratitude to Dr. J. M. H. MacLeod, for his kindness throughout my work in the pathological laboratory of the Charing Cross Hospital Medical School.

REFERENCE.

MACLEOD, J. M. H.—"The Persistence of Prickles in the Horn-cells of the Human Epidermis," *Brit. Journ. Derm.*, 1899, vol. xi, p. 137.

RAUSCH, H.—"Tinktorielle verscheidenheiten und Relief der Hornzellen," *Monats. f. prakt. Derm.*, 1897, xxiv, p. 65.

THE TREATMENT OF SYPHILIS.

By MAJOR H. C. FRENCH, R.A.M.C., WOOLWICH.

(Concluded from page 362.)

THE following research work which I undertook for the War Office in 1905-6 on three samples of mercurial cream kept at uniform temperatures in an incubator may prove of interest. The research is mainly of a chemical nature, but the therapeutic action of insoluble grey oil in the treatment of syphilis has been closely watched during the past three years.

Mercurial Cream.

	A. For temperatures 70° to 80° F.	B. For temperatures 80° to 95° F.	E. For temperatures 90° to 105° F.
Hydrarg. pur	2 drachms (by weight)	2 drachms (by weight)	2 drachms (by weight)
Adeps lanæ anhydrous .	3 drachms (by weight)	3 drachms (by weight)	3 drachms (by weight)
Paraffin Liquid, Carbol. } 2 per cent. ad . . . }	10 drachms (by measure)	—	—
Paraffin Molle, Alb. } Carbol 2 per cent. ad }	—	10 drachms (by measure)	—
5 minims contain 1 grain of metallic mercury.			
Dose, 5 minims.			

REPORT ON THREE SAMPLES OF MERCURIAL CREAM.

A form.—When exposed to a temperature of 70° to 80° F. the metallic mercury separated out and sank to the bottom. If the pot is placed in boiling water and stirred the mercurial cream in *A* form is fit for use in three minutes, and remains so for fifteen minutes, when it requires heating again. This form readily passes through the needle. The three samples of this form have been used.

B form.—When exposed to a temperature of 80° to 95° F. the metallic mercury separated out and sank to the bottom as in Form *A*. When *B* form is placed in boiling water the mercurial cream is fit for use in five minutes, and remains so for ten minutes if taken out of the hot water, when it requires heating again. This form is not so soluble as *A*, and apparently more suitable for climates warmer than England. The three samples of *B* form have been used.

E form.—When exposed to a temperature of 90° to 105° F. the metallic mercury separated out as in *A* and *B* forms.

When *E* form is placed in boiling water the mercurial cream is fit for use in eight minutes, and will only remain so for five minutes if taken out of the hot water. If used in this country it requires to be kept in hot water the whole of the time when in use. It is extremely insoluble, and difficult to get it to pass through the needles except when nearly boiling—probably not suitable for even tropical use. It was necessary to stop using it before the sample bottles had been finished. The “chronic intermittent” plan of intra-muscular injection has been used with all three forms—that is, six weekly injections of gr. j Hg., rest for three months, then six weekly injections, and so on for two years. I have not seen any case of mercurial stomatitis under the use of the “chronic intermittent” plan. Owing, however, to the frequency and persistence in many instances of marked glandular enlargement amongst out-patients, and the not infrequent occurrence of severe relapse, the total effect on the early stages of syphilis of “insoluble” salts of mercury is not always apparent amongst out-patients. I have not seen a single case of nodosity or abscess result from any of the forms *A*, *B*, or *E*, and this is solely due to asepsis and care. With *E* form, however, apart from the insolubility, several men stated that it made them feel very ill. This is attributed to the accumulation in the tissues at the site

of injection, and sudden elimination, but largely accentuated by beer drinking, irregular habits, and smoking whilst out-patients. The foregoing report was made two years ago. I have studied the action of grey oil to date (August, 1908), and the effect on syphilis is, in my opinion, of a negative character.

At Woolwich, the method of inunction which I use for in-patients is on the general lines of Aix-la-Chapelle, modified by service conditions. I substitute barley-water for sulphurous spring water in order to assist elimination by the kidneys and to guard against albuminuria—which is rare in syphilis, except in severe cases which have not come under notice early, or have not received adequate treatment. The method requires the daily supervision of an officer, orderlies are trained, and patients instructed how to use the glass rubbers either on themselves or on one another. Soldiers, as a general rule, are not too weak to do all that is requisite. The patients use condemned hospital flannel underclothing, which is changed once a month and then destroyed—so the cost is very slight. A hot bath, with plenty of soap and water, is used every morning before the inunction, which latter lasts half an hour, and takes place at 10 a.m. The skin looks like blacklead when the ointment has been thoroughly rubbed in. Forty inunctions of 1 drachm ung. hydrarg. B.P. compounded with lanoline or ung. paraffin flav. 1 drachm, or other substances, form a course. Each man is provided with the exact measured quantity. I omit the inunctions on Sundays. After twenty to twenty-five inunctions when thoroughly done the teeth may, in some instances, especially if at all carious, feel tender on eating. I usually stop for a week and give potass. iodidi in doses of gr. x, three times daily, and then finish the course. In severe cases it is wiser to give fifty to sixty inunctions with judgment. All carious teeth should be attended to prior to the commencement of a course. A mouth wash of acetate of alum is used in each case during the inunction course every two hours by day, and a soft tooth-brush is used twice daily. The groins and armpits are closely shaved, and must be kept so in order to guard against mercurial pustulation, which can usually be obviated by care and attention. I select the groins, inner sides of thighs, and armpits owing to the greater frequency of glandular orifices in these situations and so better regulated absorption, as well as for the fact that the

glands in these situations are ordinarily much enlarged and must be reduced before there is any question of suspending vigorous mercurial treatment. The glands are no doubt the repositories of syphilis, and when thoroughly reduced are capable of asserting their normal depurative and other functions. In early syphilis the glandular tissue of the tonsils is ordinarily first hypertrophied and congested, although later in the disease the tonsils may atrophy or disappear. As cases of syphilis vary so much in variety and intensity, no hard and fast rules can ever be laid down as to treatment. One man may require mercury, another food, another tonics. I find no other method of treatment in the initial chancre and rash stage, say the first six months from contagion, that is so generally valuable as inunctions, but the method requires experience and detailed personal attention. I think that a syphilised person should always receive two courses of forty inunctions within the first six to nine months, and if practicable four courses in the first eighteen months. After the first two courses mouth treatment will ordinarily suffice to guard against relapse. Hydrarg. cum creta with opium in small doses, as recommended by Hutchinson, acts well in guarding against relapse, alternating with tonics, potass. iodidi, or other remedial measures according to the particular indication or the individual case. In many cases hydrarg. cum creta will fulfil all necessary requirements throughout the case, but in the light of later experience I believe that I am more thoroughly treating syphilis by using the inunction method with daily bath whenever practicable in early syphilis. According to the evidence of the Advisory Board reports inunctions are used in the French, German, Austrian, Bavarian, and other armies as the routine method of treating syphilis. The method is in use at Aix and Wiesbaden and at other clinics on the Continent. It can be understood, however, that the excellence of this method can only be tested amongst in-patients under restrictions, such as exist in military life—and that in civil hospital practice, or private practice, this treatment may be difficult to arrange. Mouth treatment is ordinarily only used on the Continent to guard against relapse—and to meet the convenience of patients—just as in the British Army grey oil injections are largely used for convenience and to meet the service requirements of out-patients. In the late secondary and tertiary stages administration by the mouth acts well of preparations,

such as liquor hydrarg. perchlor. in combination with potass. iodidi, or the biniodide of mercury in solution, as the digestion is not at this period so easily disturbed as in the initial congestive stage of syphilis. Grey powder with opium acts well in the primary and early secondary stage, and is strongly advocated by Mr. J. Hutchinson. Opium is a valuable ally with mercury, as it checks diarrhœa and promotes diaphoresis. Mr. Hutchinson considers that inunctions are very valuable, but that grey powder is more convenient for private practice. Calomel vapour baths are best suited to severe external lesions such as marked papular or pustular lesions and ulcerating gummata, which may resist other methods. They should not be too long continued, as mercurialisation may be rapidly induced owing to the large extent of skin surface from which absorption is taking place. I employ Lee's vapour bath in all severe cases, either with or without calomel, according to the necessities of the individual case. I usually give about ten baths, the baths taking place every other day with $\frac{1}{2}$ drachm of calomel for each bath. The drug must not be wiped off from the body. The Zittmann treatment, which consists of mercury in minute doses administered in a small room in which the patient remains, was well thought of by the late Sir Alfred Cooper, and the method is fully discussed in his work on syphilis. It is suitable for cachectic emaciated cases or cases of malignant syphilis who do not react to ordinary remedies. A room for this class of case is being built at Woolwich and at Rochester Row, London. Some foreign invalids, who weigh only six to seven stone, are unable to take any specific treatment, or eat ordinary food. The reported results in malignant syphilis are very favourable, as much as a stone in weight being put on. Hot-air electric baths would no doubt serve the same purpose. The patient must be built up first and local measures are essential. No doubt change of air is of great value, but general treatment is equally important in all grave cases. Milk, eggs, and port wine should supplement the ordinary diet. The duration of administration of mercury is in some measure dependent on the type of constitutional disease, on idiosyncrasy, and on the general health of the patient. I object to any method of pushing the drug and making the patient fit in with the treatment. I have seen men broken down by mercury as well as by syphilis, and this condition may be most difficult to put right, and it is then not easy to convince the patient

that the remedy is of value. If the drug be given until the gums are touched, mercurial poisoning may easily occur. This danger is largely guarded against by the prior treatment of carious teeth by astringent gargles, such as acetate of alum, and by daily hot baths. If mercurial stasis occurs, and a blue line appears on the gum, or if the gums be spongy and the tongue swollen, stop the drug at once. Give soft food and stimulants, hot baths, paint the gums with a solution of gr. x to the ounce argent. nitratis, and give a weak permanganate of potass. gargle every hour. It is my practice to give mercury more vigorously in the first than in the second year. If the patient is robust, and the attack severe, as evidenced by an infiltrated papular or pustular rash, with or without iritis or alopecia, and marked glandular enlargement, a larger quantity of mercury in the early stages is well tolerated by a carefully dieted patient in hospital. If, on the other hand, the infection is a mild one, as evidenced by a non-infiltrated roseolar rash and slight adenitis, or if the patient is nervous or debilitated from any cause, or has carious teeth, a much smaller dose may be badly borne. As a rule mercury should be efficiently, invariably, but intermittently given for twelve months, although the first nine are much the more important, with gradually increasing longer intervals in the second year, and combined with mixed treatment with potass. iodide or tonics during the intermissions according to the general condition. No hard and fast rule as to dosage can ever be laid down which would suit every case, but the merits of each must be absolutely decided by the experience of the individual practitioner.

Owing to our ignorance of the laws of assimilation and elimination it is unwise to give the patient in any stage as much mercury as he can stand, because this practice, though advocated by some persons, constitutes an abuse of the drug, and may result in mercurial stomatitis, or mercurial stasis and poisoning, from at first being unduly accumulated and later too suddenly eliminated. This would affect the general health, which is a most important consideration, as the manifestations of syphilis are usually in inverse ratio to it. Treatment should, I think, be directed towards enabling the patient to take the drug by regulating elimination, and inducing an increase of metabolism by baths, food, and general exercise in the fresh air. If the bactericidal properties in the blood are to effect the cure of syphilis, this must necessarily result

from increased metabolism due to the careful administration of mercurial preparations. As a result of such administration the lymphatic glands become reduced in size and so continue their depurative and eliminatory function. When they fail they break down and suppurate. This result is not infrequently seen in neglected or badly treated syphilis. Too long a continuance of a large dose in any form creates a markedly retrograde effect, and gives rise to anæmia, loss of weight and general condition, as well as acting as a systemic poison, and probably prevents anti-bodies forming in the blood. The factor "general condition," when adequately maintained, has no doubt as powerful an effect as the mercury in improving the status of the red blood-corpuscles, and in eliminating the syphilis by improving the tone of eliminating organs, such as the liver, kidneys, and skin. "If blood-counts be made it will be found that the count of red cells and the amount of hæmoglobin increase during the first three weeks of mercurial treatment begun when secondary manifestations of syphilis have occurred. After that time if mercury is still given the hæmoglobin and, later, the number of red corpuscles begin to decline" (Cabot). Hydro-therapeutics and electro-therapeutics are useful adjuncts to a mercurial course, and a valuable complement after it. The absence of cachexia of the face is a valuable index to the progress of the case and a guide to interrupting or continuing the mercurial course. The weight is probably proportionate to the condition of the blood and to the satisfactory nature of our remedies, since great variations are often apparent in the weight of untreated and properly treated cases of syphilis. In severe cases, treated or otherwise, the weight may fall steadily for a time, and anæmia is more or less marked. A fat person, however, may lose weight and yet gain in general condition. The persistence of indurated and enlarged lymphatic glands is a most valuable sign for the continuance or otherwise of a brisk mercurial course, especially by the inunction method combined with radiant light baths, or of a substituted mixed treatment. Until the induration and enlargement of the glands is thoroughly and permanently reduced in cases of constitutional syphilis there can be no question of cessation of treatment. Under efficient treatment these glands are reduced to normal in about six to nine months from the date of infection, but in some cases this can occur earlier, and quite independently of treatment. The lymphatic glands are ordinarily normal

with tertiary lesions if we except early malignant syphilis. Intramuscular injection of insoluble grey oil is not nearly so efficacious in reducing glandular enlargements as other methods, such as inunction or hydrarg. cum creta in the early stages. Slight albuminuria occurring as the direct result of syphilis is not a bar to the carefully watched administration of small doses of mercury, but a large amount of albumen in the urine, or albuminuria the result of nephritis from other causes, is a contra-indication to the use of the drug. Mercury is often badly borne in syphilis associated with recent malaria, scurvy, or tubercle, or in any grave anæmic state. Nervous tremors occurring during the mercurial course contra-indicate the continuance of the drug.

Alcoholic subjects and persons with neurasthenic temperaments, epileptic fits, or hereditary tendency to insanity require great care. Cellulitis not infrequently attacks wounds or alcoholic syphilised subjects under active mercurial treatment, and sepsis may quickly occur after operation in the early stages. Boils, whitlows, and carbuncles not infrequently occur in association with early syphilis. Grave septicæmia may occur with necrosis of bone in tertiary phases, and treatment should be first directed to ordinary surgical procedure for the necrosis and secondarily to specific drugs.

Before iodide of potassium is administered the question of renal sufficiency should be adequately gauged. If albumen is present, or the quantity of urine insufficient, the iodide eruptions are likely to occur, and hence the value of free dilution of the drug together with hot air or electric light baths, as these exercise a markedly beneficial effect on the kidneys, and assist elimination by the skin. The headache and osteoscopic pain of early syphilis may rapidly yield to potassium iodide alone, or in combination with mercury, and a pustular syphilitic rash is markedly benefited. The drug may give rise to headache if albumen is present in the urine.

Potassium iodide is more obviously beneficial the further the stage from primary infection, and its use, therefore, is imperative in the late secondary and tertiary stages, or in any manifestations, however early, such as malignant syphilis presenting the attributes of those stages. This drug is most valuable in cases of early syphilitic orchitis, in periostitis, nodes, gummata, gummatous ulcerations, and in threatened brain or cord lesions. Patients who are intolerant of

small doses, such as gr. v, may take a larger one with impunity. The drug is best borne about an hour after meals in dilute solution in such vehicles as water, milk, and sarsaparilla. The depressant action is best avoided by prescribing it for short periods at a time of ten to fourteen days, and in solution with ammonia carbonate, also by associated tonic treatment and hot-air baths, and by administering the large dose at bedtime and avoiding its use in the early morning. It is then not so likely to derange digestion or cause depression. A course of a month once a year is valuable as a precautionary measure against parasyphilitic affections, and is strongly advocated by Sir William Gowers. The drug, as a matter of routine, should always be given as the complement of the mercurial course, since it is generally believed to assist in the gradual elimination of the accumulated mercury, and so guard against mercurial stasis and poisoning. It also acts, especially when combined with sarsaparilla, by relieving the liver and kidneys, which may be chronically congested or lardaceous. The drug can remove the barricades of nascent fibrous tissue in which the syphilitic virus or its toxin is no doubt lodged in latent and later stages, and thus permits the leucocytes to enter and effect the removal of the virus or its products, and this explains the lessened anæmia of the patient in suitable cases. The drug often rapidly reduces the enlarged glands. The moderate use of the drug, therefore, causes a more healthy tone of tissues, blood, lymphatics and organs, which can then more naturally overcome the effects of the bacillus or its toxin. In certain stages of threatened brain syphilis which have been neglected in the early stage mercury may prove more valuable, but commonly in "syphilis grave" or in "malignant" syphilis mercury may prove quite useless, and general condition is the first consideration.

"As a result of the apparent beneficial effects which had been obtained from the use of atoxyl in sleeping sickness, it was suggested by Uhlenhuth that this drug might also prove successful in syphilis, the latter being, like sleeping sickness, a protozoal disease."* Atoxyl has given rise to many cases of toxic poisoning as well as to many cases of total blindness in treating sleeping sickness. This is attributed to adulteration of the drug, etc., but the symptoms appear to be those of ordinary arsenical poisoning, namely "gastro-intestinal

* *Brit. Med. Journ.*, August 15th, 1908, pp. 391-394.—Col. Lambkin, R.A.M.C.

pains, nausea, vomiting, painful micturition, and painful sensations in the limbs" (*i.e.* arsenical neuritis),* these symptoms possibly being due to intra-muscular injection as can occur with insoluble injections of mercury. Soamin (sodium-aminophenylarsonate), soluble in five parts of water, is a preparation made by Burroughs Wellcome & Co., London. It is reported to have a toxicity of one fortieth that of arsenious acid and to be a safer drug than atoxyl. It contains 22·8 per cent. of arsenium (As) in organic combination. The use of arsenic in the treatment of syphilis and other skin-diseases is extremely well known. In the British Pharmacopœia, Donovan's solution (liquor arsenii et hydrargyri iodidi), has been prescribed for many years in treating syphilis, and patients gain weight on it. I commonly use it, and it is valuable in certain cases. I quite concur in the view that arylarsonates may "exert their use in strengthening the phagocytic defence of the host."† Judicious dietary, iron, quinine, sanatogen, malt and cod-liver oil in common with arsenic exert a similar effect. I do not, on the evidence presented, concur in Colonel Lambkin's view, "that one important fact has been established, that is, that in these salts (arylarsonates) we are now in possession of a *specific* for syphilis, and the importance of this cannot well be exaggerated.‡ In the very next sentence it is stated, "that they do not kill the germ as mercury is supposed to do."§ Apparently thirty cases in all were treated by Colonel Lambkin with the arsenical salt soamin, but only thirteen of the "most prominent" are recorded. These thirteen cases were admitted to hospital with the initial lesions of syphilis for soamin treatment in April and May, 1908, and discharged from hospital in May and June. Up to July 30th, 1908 (the date of writing), in a period of under four months' observation no relapse is reported to have occurred. On such evidence the statement is made "that injections of soamin can be looked on as prophylactic in the majority of cases against any further development of the disease (syphilis) if given early and in sufficient quantities."|| It is necessary to remember that external manifestations in the average run of cases are comparatively rare a year from infection both in treated and untreated syphilis. This fact is generally recognised by writers on this subject. Further, tertiary symptoms, when they occur, usually do so in three

* *Ibid.* † *Ibid.* ‡ *Ibid.* § *Ibid.*

|| *Brit. Med. Journ.*, August 15th, 1908, pp. 391-394.

to five years after infection. The fact of the thirteen "prominent" cases gaining four to six pounds whilst treated in hospital by soamin for some time is very largely due, in my opinion, to the admittedly beneficial effect of rest and a generous full hospital dietary, namely "ordinary," as well as to local treatment in the early and more remediable stages of syphilis. Average cases of syphilis have a spontaneous tendency to cure under such highly favourable circumstances quite apart from treatment by drugs. I have seen ten to thirty pounds in weight thus gained even in severe cases without a grain of mercury or arsenic being used. At the present time there is a severe case in hospital at Woolwich who has gained thirty pounds within two months on general and local treatment, and numerous recorded cases can be cited of a gain of half to one stone, where previously treatment by specific drugs has been repeatedly tried and failed. How true this is in speaking of malignant syphilis is a matter of general knowledge.

Quinine in dilute acid solution is often most valuable precedent to, or after, the first mercurial course in cachectic cases. Whether it exerts a specific action on the *Treponema pallidum* as on the malarial parasite is uncertain, but I always temporarily substitute it for mercury if there is an associated malarial history or if syphilitic fever is present. As early syphilis is associated with a loss in numbers of the red blood-corpuscles and in the amount of hæmoglobin in these cells, quite possibly its chief action may be in overcoming the degenerative action, and thus assist the blood to deal with the inroads of the virus in the early and more remediable phases of the disease by increasing its phagocytic power, or by the formation of anti-bodies. Cod-liver oil and iron are similarly valuable for their hæmatinic powers. Any drug, however, or any means which tends to reduce the number of spirochaetes in the system in the early stages will consequently lessen the amount of toxin produced which can later injure the central nervous system and give rise to para-syphilitic affections.

The very greatest advantage may accrue from a cessation of mercury or potass. iodide, and the substitution of other tonic remedies. I think that this is more especially the case in alcoholic, scorbutic, anæmic, or tubercular subjects, and in malignant syphilis. There is no class of disease in which the beneficial results of judicious and early treat-

ment are so marked as in syphilis. If the remedy used is doing good the result is early apparent, and the manifestations of the disease disappear; if, on the contrary, the manifestations are stationary or growing progressively worse the remedy is inadequate and fresh methods should be essayed, either by an increase or decrease of dose, or the substitution of other drugs and remedies. The application of the rules of antiseptic, aseptic, and general surgery to the wounds of syphilis is valuable in proportion to the extent and manner in which they are used. If there are ulcers in the throat or mouth local treatment is requisite, and a minced meat or stew diet is essential to successful results. Otherwise the patient tends to lose weight if he is unable to masticate or swallow too solid food, and mercury would only aggravate matters. Success more often depends in maintaining the strength by means of the judicious use of stimulants and nutritious food than on drugs. This is especially true in cases of iritis, severe throat lesions, necrosis of bone, and in malignant syphilis.

I have merely endeavoured to suggest some of the general principles and broad lines on which the various forms of treatment may be best conceived and best maintained.

ROYAL SOCIETY OF MEDICINE.

DERMATOLOGICAL SECTION.

A MEETING of the Dermatological Section was held at 20, Hanover Square, W., on Thursday, November 19th, 1908, Dr. H. RADCLIFFE-CROCKER in the Chair.

The SECRETARY read the minutes of the previous meeting.

On a point arising out of the minutes, Dr. ARTHUR WHITFIELD made a statement upon a case reported as *rhinoscleroma* which was brought before the last meeting of the Section by Mr. T. J. P. Hartigan. He said that the sub-committee appointed to consider the case, consisting of Dr. Adamson, Dr. Bunch, Mr. Hartigan, and himself, met at his (Dr. Whitfield's) house on October 30th. Mr. Hartigan asked permission to bring Dr. Wingrave into the consultation, as that gentleman had special opportunities of examining the

case, and this was granted. As a result of the first meeting it was found that the cultures were not pure, and, unfortunately, Mr. Hartigan had lost the only specimen which showed the bacillus *in situ*. In the others the materials were not sufficient to give any decisive features of rhinoscleroma. The meeting was postponed until November 9th, when further materials for histological examination were promised by Mr. Hartigan. Just before that date, however, he informed the other members of the committee that he had not been successful in obtaining the materials, and desired that the diagnosis of the case should be unreservedly withdrawn.

A note was therefore appended to the minutes to the effect that the diagnosis of rhinoscleroma was withdrawn from Mr. Hartigan's case, and the minutes were then confirmed.

The PRESIDENT read a letter from the Secretary of the Royal Society of Medicine containing a recommendation from the Central Council that the officers of Sections should all date the commencement of their duties from October 1st, notwithstanding any previous regulation. This was agreed to.

Dr. ARTHUR WHITFIELD then read a paper on "Inflammatory Nodules of the Hypoderm" (*vide* vol. xxi, page 1).

Dr. H. G. ADAMSON showed (1) a case of *Acne scrofulosorum*. The patient was a young woman, aged 25 years. At the age of twelve years she had suffered from an abscess in the neck. The eruption had been present about three months. The lesions were scattered without any tendency to grouping over the backs of the elbows, forearms and hands. They consisted of (*a*) hemp-seed-sized, firm, dusky-red nodules, not painful nor tender; some were hair-centred, others not; a few showed a small crust at their summit; (*b*) shallow pigmented scars, obviously the remains of former papules which had crusted. The patient's fingers were cold, and she stated that she always had chilblains in the winter, but what she called chilblains were dusky indolent nodules without itching and with a tendency to central crusting and subsequent scar, in fact similar, though somewhat larger, lesions to those on the forearms. Below the jaw on the left side was an enlarged gland, and alongside an old scar, but there was no evidence of tuberculosis of the lungs or elsewhere.

Dr. ADAMSON also showed microscopical sections of lesions from five other cases of *Acne scrofulosorum* (or small nodular tuberculide), which had been under the care of Dr. Colcott Fox. The sections showed a circumscribed cellular infiltration deeply seated in the cutis, and involving a sweat-duct or a hair-follicle, or both. The infiltration was made up of (*a*) mononuclear round cells (lymphocytes) around the blood-vessels, and (*b*) epithelioid cells (young connective-tissue cells) occupying the main part of the lesion, with, in three of the sections, an occasional giant-cell. There were no polynuclear leucocytes, except towards the apex of one nodule which had broken through the epidermis.

The case belonged to the group of eruptions now generally known as "small nodular or acneiform tuberculides" or toxi-tuberculides, and formerly described in this country (by Colcott Fox, Radcliffe-Crocker, Pringle and others) as *Acne scrofulosorum*. These, or closely similar eruptions, had been described also under various other titles, such as *Hidradenitis destruens suppurativa* (Politzer), *Spiradenitis suppurativa disseminata* (Unna), *Granulome innominé* (Tenneson), etc., and the terms "acnitis" and "folliclis" had been invented by Barthélemy to distinguish regional varieties. But since all these eruptions showed the same histological structure, and as all were now regarded as small nodular tuberculides, only differing in size and situation, it seemed better to use one term for them all, either the original name "*Acne scrofulosorum*" (Colcott Fox), or "small nodular tuberculide" (Darier).

(2) A case of *vascular nævus* of unusual type. The patient was a little girl, aged 7 years, who had been kindly sent to the exhibitor by Mr. R. C. Elmslie from his clinic at the Metropolitan Hospital. A "red mark," of the size of a threepenny-bit, had been noticed at birth on the right arm close to the anterior fold of the axilla. When the child was two years old this patch began to increase in size. There was now, occupying the dome of the axilla, and extending across the anterior fold on to the arm, a red, sharply margined patch, with a slightly raised and festooned margin. At first sight the lesion suggested an erythematous patch with an œdematous advancing edge, but the history of gradual extension since birth negatived this view. No dilated blood-vessels could be detected even with a lens. On pressure most of the redness disappeared, but some brownish

stain remained. Passing across the anterior fold of the axilla was a fine cord-like swelling, buried in the red patch, possibly a large blood-vessel. A section prepared by Mr. Elmslie had made the diagnosis clear, viz. that of vascular nævus, though the vessels present were many of them evidently new-formed, and others still in process of formation. Mr. Elmslie had reported that the sections showed some small patches of cells in the sub-epithelial tissue (endothelial cells), enclosing tiny capillaries with thick wall, and containing very little blood. These patches were scanty, but they were evidently of the nature of vessels, so that the condition must be regarded as a nævus.

Dr. DORE showed a case of *psoriasis associated with recent syphilis*. Since he was eight years of age the patient had had psoriasis. Five weeks ago he had a fresh eruption of papules, and Dr. Dore diagnosed "recent syphilis on an old psoriasis basis." In addition to the eruption he had superficial glossitis and an erosion on the glans penis, but no indurated chancre. He had had a little treatment for the psoriasis. There seemed little possibility of doubt as to the syphilis.

Dr. PRINGLE said he thought psoriasis might pursue its course unaffected by the syphilis. Or the psoriasis might disappear entirely in the course of the syphilis, remaining away as long as the syphilis was present, to reappear afterwards.

Dr. G. PERNET said he had seen psoriasis unaffected by syphilis, but he thought the former became more inveterate from the association.

Dr. COLCOTT FOX and Dr. GRAHAM LITTLE expressed some doubt, in the absence of the hard chancre, as to the existence of syphilis in this case, and did not feel satisfied that the symptoms could not be explained by psoriasis alone. Dr. Little suggested that a biopsy of one of the recent papules claimed as syphilitic should be undertaken. He had had a similar case of association of the two diseases in which a biopsy had cleared up all doubt as to the addition of syphilis to the old psoriasis.

Dr. JAMES GALLOWAY and Mr. KENNETH GOADBY demonstrated an unusual *bacillus* found in the lesions of a case of *rosacea*. Dr. Galloway said that the patient in whose case these observations had been made had been brought to see him in June of this year by Mr. Goadby. She was a lady, aged about 46 years, who had, for a period of about seven years, suffered from a slight degree of rosacea. In addition there had been slight disturbances of digestion with some

tendency to functional nervous manifestations, but with these exceptions she was in good health. The eruption on the face consisted of attacks of slight transient erythema of the central portion of the face; in places this erythema was more persistent; only a slight degree of permanent dilatation of the superficial blood-vessels was observed. During the past two years, in addition to these vascular changes, there appeared on the face an eruption consisting of sparsely scattered papules of a dusky red colour. These were slow in developing and lasted for some weeks. Usually a small quantity of sero-pus formed in their interior, and subsequently the little tumours disappeared. The recurrences of these lesions were frequent and caused a good deal of trouble to the patient. This type of eruption complicating rosacea would be familiar to Members of the Section; cases had been shown by Dr. Pringle, Dr. Colcott Fox, Dr. Galloway, and others at the Dermatological Society of London (*British Journal of Dermatology*, vols. vi, p. 368, xiv, p. 162, xv, p. 41).

Mr. Goadby had made a careful bacteriological examination of the sero-pus obtained from the lesions, and had obtained a bacillus at first contaminated by the white staphylococcus, but now in pure culture. Mr. Goadby had been able to obtain this bacillus repeatedly from the lesions. It was found to be slightly pathogenic to animals, and had been recovered in pure culture from the lesions produced experimentally.

Mr. Goadby had treated the patient carefully by means of a vaccine prepared from this bacillus; the vaccine provoked a reaction in the lesions, but had no curative effect.

Dr. Galloway remarked that he was unable to identify the bacillus isolated by Mr. Goadby, and Mr. Goadby himself had been unable to identify it with any of the organisms usually found under such conditions. It was, therefore, thought advisable to show the micro-organism to Members of the Section.

The patient, on consultation, was treated by means of local applications of sulphur to the face, and attention was paid specially to the condition of digestion and her general health.

Dr. Galloway was glad to be able to report that the eruption had disappeared and that the patient was now in good health.

Mr. Goadby said cultivations were made from the small pustules on the face from several positions—the alæ of the nose, the chin, and

the tip of the nose. The lesion had already been described by Dr. Galloway, and needed no further comment. It sufficed to say that underneath the thickened portions of the skin in some places pus was obtained, small in amount and rather greasy in consistency.

Cultivations were made from the pus on several media, glucose formate broth (anaërobically), agar, serum agar, broth, and blood-serum. The cultures were grown at 37° and plated at the end of forty-eight hours.

A considerable number of colonies developed from two of the plates made from the direct cultures of the pus, but not all of the tubes made directly from the lesion showed growth.

Microscopic examination of the tubes containing the direct smears showed a mixture of organisms, bacilli and cocci.

The colonies on the agar plates looked somewhat the same, and it was a little difficult to determine the difference between the two species of colonies. The colonies of bacilli, however, were rather drier and browner than those of the staphylococcus present. On the gelatine plates the colonies of bacilli were iridescent by transmitted light, but white by reflected light.

The cultural characters of the organisms were as follows :

Bacillus 3 to 5 μ long, and about 1 μ broad. It was not motile, and it did not stain by Gram's method. Stained by carbol methylene blue deeply-staining blue dots appeared in the organism, whilst stained with carbol fuchsin the spots which took on the stain deeply with methylene blue remained as whitish points.

No spores were found to be present either by staining or by the method of heating old cultures and testing the growth. The thermal death-point was found to be 56° C. for twenty-one minutes.

Agar.—On agar the growth was regular, of a brownish-grey colour, and smooth and somewhat moist.

Gelatine.—On gelatine well-marked "nail growth" of a porcelain white colour occurred, but no liquefaction of medium took place.

Streak.—On the streak a well-marked greyish-white coloured growth resulted with a flat edge, and often discrete dotted colonies along the line of the streak.

Broth.—A very slight general turbidity was produced at the end of forty-eight hours, and a very slight precipitate, which was of a stringy nature, on rotating the tube, rose up as a small tenacious string.

Blood serum.—The organism grew well on blood-serum and blood-agar; no liquefaction of the blood-serum took place.

On the carbohydrates tested little acid and no gas were produced, and no change took place in any of the media until the fourth day. At the end of this time glucose and sorbite showed a slight acid reaction, whilst there was a slight trace in the salicin tube. Lactose, maltose, cane sugar, inuline, caffeine, mannite, and dulcitol all showed no change.

Anaërobic cultures.—Very slight growth took place on anaërobic media. On glucose formate agar, in Buchner tubes, a slight development occurred.

Animal experiments.—Two guinea-pigs were inoculated with a whole agar culture of the organism twenty-four hours old.

In one case a slight local reaction occurred, the swelling remained for about a week, and the hair did not grow over the swelling. A small proportion of the contents were removed with a sterile pipette, and the organism was recovered in pure culture. The sides of the abscess did not break down, and the animal entirely recovered.

In the case of the other animal, slight local swelling persisted for two or three days and then rapidly disappeared. The organism was not tested on any other animals.

Staphylococcus albus was the other organism present in the cultures isolated from the face. This organism is perhaps of little importance, as it is known to be commonly present on exposed surfaces of skin, and may frequently be met with in the deeper layers of the epidermis.

Result.—The patient, previous to being seen by Dr. Galloway, had been inoculated with killed cultures of the bacillus in question. The opsonic index in the first place was 0·5, and after the inoculation a considerable amount of increase of the local affection of the face took place, followed by a good deal of improvement. The condition, however, did not clear up entirely, and although the opsonic index was raised to a considerable pitch—2·4, no lasting improvement resulted, and when the patient saw Dr. Galloway there was still present in the deeper-seated areas of suppuration the same bacillus in company with the staphylococcus.

Vaccine used.—The vaccine used was a combined vaccine of the staphylococcus and the organism.

The photographs show the curious beaded appearance of the organism when stained with carbolic methylene blue and carbolic fuchsin.

I have been unable to discover any reference to this organism among those described as present in skin infections.

The absence of any smell in the cultures excludes several bacteria, such as *B. graveolens* of Bordoni, *B. ovatus*, Unna and Tommasoli, *B. Spiniferens*.

Bacillus erythematodes does not grow on gelatine.

The organism has some of the characters of *B. catarrhalis*.

Bacillus epidermidis or *Leptothrix epidermidis alba* is without the curious staining properties I have mentioned, and is a much larger, longer organism and stains by Gram's method.

Bacillus folioformis stains by Gram and produces yellow pigment.

Dr. WHITFIELD said that he was familiar with the bacillus found by Mr. Kenneth Goadby. He had obtained it in making vaccines from *Acne vulgaris*, and in the particular instance in which he remembered getting it in large numbers the pus had come from deep acne pustules on the back. He had regarded it as an accidental contamination and had rejected vaccine in which he had found it. The reaction of the local skin condition would only be of diagnostic significance if the bacillus were used in pure culture as a vaccine.

Dr. EDDOWES advised that search for the organism should be made in rhinophyma. He believed it was not peculiar to rosacea. In both those diseases there was a great tendency to an increase in fibrous tissue, instead of to breaking down. And the present contribution might be a help in regard to treatment, because if it was an active organism which was the cause, instead of soothing applications and measures to contract the blood-vessels local antiseptics should be used.

The PRESIDENT remarked that these cases were not ordinary cases of *Acne rosacea*. The Section was much indebted to Mr. Goadby, whose investigation showed how much useful work yet remained to be done in the bacteriology of the skin.

Dr. GRAHAM LITTLE showed (1) a case for diagnosis. The patient was a house-painter and decorator by trade, but denied contact with the covered parts of his body of any irritant such as the materials used in his trade. The eruption appeared suddenly, being first noted exactly four days before the date of his being shown, upon his supra-pubic region and then on the thighs, at first in the form of discrete papules, which did not itch and which rapidly became confluent, so that the skin from the supra-pubic region to the thighs was a uniform inflamed surface. When shown, on November 19th, there was a continuous sheet of

inflammation occupying the whole space between the pubes and the umbilicus, the lateral boundaries of this area of disease being found in the vertical line drawn through the middle or outer third of Poupart's ligament; the pubic region itself, covered with hair, and the scrotum were quite free of disease, but the inflammation extended in a continuous sheet from the fold of the groin to the knee, occupying the whole of the inner aspect and the inner half of the anterior surface of both thighs and both popliteal spaces and the skin over the calf. These areas were covered partially with white thin scales, which were easily detached, and left when removed an intensely erythematous but dry surface of a deep bluish-red colour. At the outer margin of the patches of continuous redness there were numerous isolated follicular papules which remained discrete. The eruption was stated by the patient to have commenced with similar papules. The eruption had never been itchy and had always remained dry throughout. No other parts of the body than those described were in any way affected; the hands sweated freely and the skin of the palms was, perhaps, a little unusually thickened, but there were no follicular papules on the dorsal aspect of the phalanges and the extensor surfaces of the joints were quite normal. There were no lesions in the mucous membrane of the mouth.

The discrete papules were rounded and varied in size from a pinpoint to a split pea; there were no lichen-like lesions, but all were acuminate, slightly horny follicular papules. The patient had applied no local measures, and had taken no drug prior to the onset of the eruption. He had no subjective symptom in connection with his disease; he was somewhat tremulous and nervous and refused a biopsy.

The PRESIDENT said he regarded the case as one of Pityriasis rubra pilaris, a view in which Dr. Colcott Fox concurred. Other suggestions were that the disease was Lichen planus, and it was desired that a biopsy should be obtained and the case reported upon later.

(2) A case of *von Recklinghausen's disease*.—The patient was a lad, aged 12 years, somewhat undersized for his age, but of good mental development (he was in the fifth standard at his school). The history given by the mother was that he had had since birth a number of dark, coffee-coloured patches of pigmentation, varying in size from

that of a half-crown to that of a threepenny-piece, and found chiefly on the back of the trunk. There was also some diffuse pigmentation of the groin and the neck. Two years ago he began to get small swellings, the first on the wrist, which later disappeared, then one which still remains, the largest—it is now the size of a small walnut—on the skin above the head of the left radius. Numerous other and smaller nodules have appeared from time to time since that date. The smaller tumours are harder than the larger, are bluish in colour, and are found chiefly over the trunk, especially the chest, on the upper arms, and the left thigh. The nodules were quite painless, even on pressure. The nerve-trunk of the ulnar nerve did not appear thickened, and there were no fusiform swellings perceptible in its course.

It was a moot point to what degree the several symptoms of pigmentation, tumour formation, and nervous phenomena were required to be present to constitute von Recklinghausen's disease. It was probable that fibrous molluscos tumours with no other symptoms could not be accepted as coming within the definition of the disease; nor could pigmentation alone be a sufficient symptom. It was nevertheless interesting to note that in this case the pigmentation had preceded by about six years the development of tumours. The exhibitor had seen at the last meeting of the Clinical Section of this Society two cases of von Recklinghausen's disease, so called, one of which he had been able to bring to this meeting by the kindness of Mr. F. E. Fenton, who would show the case, which tallied closely with the case just described and which had improved markedly with injections of fibrolysin.

Mr. FENTON (introduced by Dr. LITTLE) showed a case of *von Recklinghausen's disease treated by fibrolysin*. The patient was a woman, married, aged 52 years. At the age of sixteen she noticed several small nodules under the skin on her back and chest; from this time there had been a gradual increase in their number and size. There is no evidence that it was hereditary. In May last, when the patient first presented herself, there were between two and three hundred tumours distributed over the whole of her body and limbs. In size they varied from a pea to a walnut or an egg, most of them hard nodules beneath the loose skin, others round and imbedded deeply

under the skin, while others were pedunculated. Over the sacrum and on each hip they were ulcerating and even sloughing.

Treatment.—About forty of the largest tumours were excised, the pedunculated ones being ligatured. Fibrolysin was injected hypodermically every third day for the first fortnight, and once a week for the next two months. After the first five injections there was distinct softening, and gradually all the tumours softened and contracted; the dose was 2·3 c.cm. and was made into the connective tissue of the back.

Dr. RADCLIFFE-CROCKER showed, for Dr. LITTLEJOHN, a case of *Acrodermatitis perstans* (Hallopeau) in a female. The patient, he said, was suffering from chronic melancholia, and was an inmate of Hanwell Asylum. He (Dr. Crocker) was responsible for the diagnosis. A case had been shown in this country by Stowers, and there were a few cases on record by Frèche and others. The disease had a tendency to spread from the finger-ends upwards, but it seldom went beyond the ends, and it was extremely liable to relapses and recurrences. The toes were apt to be affected.

In answer to Sir Malcolm Morris, who asked whether there was any peripheral neuritis, Dr. Crocker said that he was not aware of it. He added that the disease was somewhat allied to what he had described as *dermatitis repens*, but at the same time had distinctive differences. That disease spread peripherally, but it did heal and did not tend to recur. One did not get relapses in the old cases as one did in these. *Acrodermatitis perstans* was characterised by its persistence and tendency to constant spread. He had had a case in private which was, so far as he knew, cured by persistently soaking the nails in lead lotion, and afterwards doing them up with linseed ointment.

In reply to a further question, Dr. Crocker said that a cultivation was taken two days before, and if the treatment he had described was not successful they would see what vaccination would do.

Dr. J. J. PRINGLE said that a considerable number of such cases occurred, although usually of much less intensity than the one shown. His impression, as a result of a study of similar cases for many years, was that it was an acrodermatitic eczema. In the first instance there was a good deal of pain complained of in the fingers, occurring usually in hysterical and neurotic women, and not infrequently accompanied by essentially neurotic disease. He believed

that owing to the disease the nutrition of the skin was impaired, giving rise to pus cocci. He suggested that permanent immersion in a hot concentrated boric solution would very likely do considerable good in this case. He believed the disease to be quite a minor one, accompanying one or other of the diseases roughly classified as neurotic. He (Dr. Pringle) had written a description of it in Quain's *Dictionary of Medicine*.

Sir MALCOLM MORRIS showed (1) a case of *leprosy* treated by Dr. Nicholls with a special vaccine, and by Dr. Dore with X-rays.

Family history.—The father died of dropsy when the patient was two years of age. The mother was alive and suffered from diabetes. Four brothers and one sister were healthy.

Personal history.—Previous to his present illness the patient has always been healthy, and has never been in contact with anyone suffering from a similar complaint to his own. He can only attribute it to the fact that he had been much bitten by mosquitoes.

The patient, aged 24 years, was born in Mauritius and lived there nineteen years; he came to England in August, 1903, at which time he was in good health. His illness began two years and eight months ago, the first thing he noticed being "a small pimple like an acne pimple" on the left side of his face near the eye. He opened this pimple on several occasions with a needle, which he thought might have been infected, because instead of healing the pimple increased in size, and soon after he noticed small lumps, "like mosquito bites," in the skin of his legs.

These subcutaneous nodules were preceded by a feeling of dryness and irritation of the skin, especially of the lower extremities, and led to a good deal of scratching. They increased in number for a short time and then remained stationary. In September, 1906 (six months after the first lesion appeared), nodules began to form near the eye and on other parts of the face. He was then given iodide of potassium internally, and during this treatment fresh lumps appeared on his hands; the first crop of nodules, which was attributed to the iodide, disappeared but was followed by others.

At the present time his face, wrists and hands, feet and legs are the parts chiefly affected. The face is studded with groups of rounded nodules of varying size, these being mostly small and closely aggregated on the forehead and left ear, and large, prominent, and more isolated on the cheeks, nose, lips and chin.

On the back of the hands and wrists the nodules are large and confluent; those on the legs began to improve in September, 1907, and have now to a large extent disappeared.

Vaccine treatment was begun at the Seamen's Hospital, Greenwich, by Dr. Nicholls, pathologist to that institution, on March 30th, 1908, and the patient has had thirty-three inoculations up to the present time. According to his own account he feels stronger and better in health as a result of the injections. Several nodules have disappeared, and others have become smaller and flatter.

On October 9th and 10th pastille-doses of X-rays were given to the cheeks and dorsal surfaces of the hands, with the result that at the end of a fortnight all the nodules treated were smaller and flatter, and some of them were entirely removed; others broke down and ulcerated. A noticeable reaction occurred only on the left cheek ten days after the exposure, resulting in slight redness of the skin and slight increase of the body temperature (100° F.), and on this part the improvement was more marked. The nose and left ear were exposed to the rays, and the left side of the face was given a second pastille dose on November 5th, and on November 16th the dorsal surfaces of the hands were again treated in a similar manner, the effect not having yet made its appearance.

X-ray applications.—October 9th, both hands; October 10th, right and left cheeks; October 23rd, forehead; November 5th, both sides of nose, left ear and right cheek; November 16th, both hands.

Note by Dr. Nicholls.—The study of personal immunity has attracted a large amount of attention lately, and that the opsonic index is a factor in this is undoubted. That we can act upon this index by means of so-called vaccines is certain. Unfortunately there are numerous other matters in the question of immunity to disease which render some of the efforts with vaccines less efficacious than might have been expected.

The great difficulty with vaccines in leprosy is, that so far we have been unable to grow the organism on artificial media in sufficient numbers to make a vaccine of much potency. Several men have claimed to have cultivated the organism, but their statements have not been confirmed.

Rost states that he has grown it on salt-free media. I have made several attempts, but they have been negative.

Work by Deycke has lately been published, in which he states that he has cultivated a streptothrix from the tissues under the lepra nodule by first incubating the tissue in saline solution. This I have also tried, with no results. I have attempted to cultivate the organism by using media made from skin and nerve extracts, on media containing glycerine and fatty acids, and on media that had previously been culturing other organisms derived from this patient, from the suggestion that the lepra bacilli depended upon the changes brought about by other organisms, *i. e.* that it is symbiotic. Yet every attempt with every variety of media has so far failed.

I have, however, been able to obtain a vaccine by means that I am about to describe, from which I have injected doses containing up to 300,000,000 organisms. In almost all infections doses of this magnitude would cause a very great reaction. Unfortunately, in leprosy, although some reaction takes place, it is not as great as it would be in other diseases.

In preparing this, a small nodule is selected; a skin incision is made down to the nodule, which is removed together with a quantity of the surrounding subdermal tissue, and it is needless to say that great care must be taken that there is thorough asepsis.

This tissue is placed in a tube of glycerinated broth and incubated for a fortnight. The broth and tissue is placed in a shallow vessel and slowly desiccated; the dried mass is now finely powdered in an agate mortar, a suspension is made and the bacilli counted by the usual method of comparison with blood.

If sections are made from tissue that has been incubated in this manner, it will be found that the bacilli have proliferated and completely overgrown the tissue. The bacilli are somewhat less acid-fast than those taken direct from the tissues, also most of them have a very fragmented appearance, as you will see by examining the specimen shown.

I have attempted to control injections of this emulsion by means of the opsonic index, but I find that the technical errors, due to not being able to obtain a good emulsion, are so great that the results are of very doubtful value.

Sir Malcolm Morris kindly giving me permission to use this vaccine, I injected the first dose consisting of 50,000,000 organisms, which had been heated to 60° C. as a precaution that none were living.

This injection was given on March 30th, 1908, and caused the temperature that evening to rise to 101.2° F. It had not previously been higher than 100.4° F.

I started by giving these injections every four days, regulating the dose so that there usually occurred a rise of temperature of half a degree higher than would otherwise be expected. Since last June I have injected the patient every week or ten days, according to the reaction that appears to take place. The largest dose has been 300,000,000 organisms.

During the whole of this time there has been a temperature which in the evenings was usually 100° – 100.5° F., and in the mornings about 99° F. The injection sends the temperature up to 101° F., but on a few occasions it has been much higher.

From May to October, 1908, no fresh nodules appeared, and a large number of those that were present disappeared, especially on the legs, elbows, forearms, and the right side of the face. The appearance of the patient has changed, the nodules, instead of being firm, have in most cases become soft and of a bluish-red appearance, and they tend to become secondarily infected with staphylococci and then break down; the resulting ulcers quickly heal.

The bacilli taken from different parts of the patient in most cases show much fragmentation of their protoplasm; this was not the case when I first saw the patient, the organisms being then uniform in staining. Where the ulcers have healed there is difficulty in finding bacilli, and those that are found are in a very degenerate condition.

Recently, however, one or two small fresh nodules have been noticed by the patient, but these have not shown the tendency to increase to the size of the original nodules. There has not been the same rise in temperature after each injection of vaccine. Whether or not this means that the vaccines are ceasing to have an effect I do not know.

There is a great difficulty in deciding the value of new remedies in most diseases, and leprosy is no exception, for it shows natural tendencies at times to improve, but in the nodular variety this is rarely long maintained. This patient states that in the summer months he had previously become worse, and improved in the colder weather, but under the injections this summer he has obviously improved both in general health and in the condition of his skin.

There are enormous numbers of lepra organisms present in each nodule, and it is obvious from the small degree to which they affect the health that they produce no exotoxins; consequently it would be useless to prepare a serum.

Their endotoxins are probably less than even in the tubercle bacilli, and consequently we should hope for no better results than in the case of injection of tuberculin.

Sir MALCOLM MORRIS said that he thought great credit was due to Dr. Nicholls for his successful work in this case. He did not know of anything else that would have produced such a result.

Dr. RADCLIFFE-CROCKER said that he recollected the case previously being shown before the Section. At that time the lesions were very much disguised by the iodide. He agreed with Sir Malcolm Morris as to the credit due to Dr. Nicholls in this case, but he said that there were other things which would produce remarkable results. Mercurial injections—perchloride of mercury—would bring about a remarkable result, as he had proved in cases of his own. The drawback was that one did not get cures with mercurial injections, but simply diminution of the infiltration. Certain sera had been used in some cases, but this appeared to be a new method. He thought that the case represented a distinct step forward, and the result was encouraging for further work. Those who were able to get hold of the material would doubtless try the method.

Mr. T. J. P. HARTIGAN said that about six months ago he showed a leprous patient treated by Deycke's method, and the improvement was such as could hardly be credited.

In reply to Dr. Pernet, who asked if iodide had been excluded, Sir MALCOLM MORRIS replied in the affirmative.

Sir MALCOLM MORRIS showed (2) a man, aged 48 years, who had suffered from a *rodent ulcer* on the right side of his nose for fourteen years. For the first twelve years there had been no treatment and the disease had been slowly spreading. Two years ago it was treated by electrolysis without advantage. When seen first on September 16th of this year there was a well-marked circular patch with raised hard edge with a circular ulcer covered with a scab. The scab was removed and the whole patch was covered with radium, 25 mg. On November 4th the large crust caused by the radium was removed and all trace of the disease had disappeared.

In reply to Dr. Crocker, who asked whether the radium treatment was limited to the single application, and whether the ulcer was the same size as the scar, Sir MALCOLM MORRIS said that there was but the one application, and that the ulcer was exactly the same size as the scar.

Sir MALCOLM MORRIS showed again (3) a case of (?) *Veldt sore*, shown at the last meeting, with microscopical specimens.

Sir Malcolm Morris said Mr. Bishop Harman had written a thesis on Veldt sore, and he was present at the meeting and would speak on this case. The patient had an ulceration, which had been healed by the application to it of X-rays, and the question was whether the primary disease was Veldt sore or not. One condition which the exhibitor had had in mind was an unusual form of *Mycosis fungoides*, as it was not an ordinary simple ulceration. The diagnosis was still in doubt. During the South African War he saw a number of officers with Veldt sore. In the first place there must be, as confirmed by Mr. Harman, a vesicle or bulla, but in the present patient there had been nothing of the kind. The primary lesion in this case was a rough, dry plaque.

Mr. BISHOP HARMAN (introduced) said Veldt sores were frequently multiple, and he showed pictures of the disease. He had only found the streptococcus in one case, and then it was of a definite character, in pure culture. It was extraordinarily tough, and very difficult to kill. He inoculated himself with the organism, and recovered it again from himself. He had counted as many as twenty such sores on one man, but in every case he had seen it began with vesication. He suggested that the organism should be called *Micrococcus vesicans*. The hair grew afterwards on the region affected by Veldt sore. The distribution in the present case was not like that of Veldt sore, neither did the latter last so long as here.

Dr. DORE said the original films which he had from the ulcer showed a diplococcus which Mr. Harman admitted was similar to that which he found. In his further investigations nothing grew but *Staphylococcus albus*. Another important point was the duration of the ulcer. Mr. Harman said in his paper that six months was the longest duration he had seen in Veldt sore, whereas the present patient had had his condition twelve years. Moreover, the paper said the Veldt sores occurred on the hands and feet, not on the abdomen.

Dr. GRAHAM LITTLE said that many years ago he had had a Veldt sore on the heel, contracted while in South Africa. It did not last more than three months. He had not regarded Sir Malcolm Morris's case as an example of this disease.

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- Dermatitis Exfoliativa**, Large Doses of Quinine in the Treatment of. W. H. MOOX. (*Journ. of Cut. Dis.*, September, 1908, p. 407.)
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- X-Rays in the Treatment of Diseases of the Skin.** H. G. ADAMSON. (*The Hospital*, October 10th, 1908, p. 33.)

CURRENT LITERATURE.

AN OBSERVATION ON THE ÆTIOLOGY OF LUPUS ERYTHEMATOSUS. E. SENGER. (*Derm. Centralb.*, July, 1908, p. 290.)

RECENTLY in the *Berliner klin. Wochenschr.* appeared an article by the author on the "Treatment of Lupus Vulgaris, with Special Reference to the Good Results Obtained by Inunction of the Lupus Surface with a Tuberculin Ointment (1.0 Alt-tuberculin in 10.0 to 20.0 Vasenöl)." There is a sharp reaction with swelling and elimination of the nodules through necrosis, etc. He says that this reaction is a specific one, and is on the same plane as the von Pirquet and the Wolff-Eisner conjunctival reaction, and can also be used as a differential diagnosis. He thinks, therefore, that if Lupus erythematosus were of a tubercular nature there should also be a similar reaction after a tuberculin inunction, but this is not the case and the result has been invariably negative. He has also given tuberculin injections and had no reaction; he therefore concludes that Lupus erythematosus is not of a tubercular nature, and that opinion of the French school is not tenable. D. F.

INOCULATION WITH REMAINS OF SYPHILITIC LESIONS.

F. SANDMAN. (*Derm. Zeitschr.*, Bd. xv, Heft 5.)

TAKING advantage of the fact that apes can be infected with syphilis, Sandman has investigated the infectivity of healed syphilitic lesions. He has vaccinated nine animals, eight from the healed remains of primary chancres and one from the remains of a papule. Although in every case the patient had been thoroughly treated with mercurial injections, and in some cases with atoxyl also, all the apes were infected. The time between the healing of the lesion and the vaccination varied from a few days to several months. Sandman regards this result as important in showing that patients are able to act as sources of infection even when they have no symptoms. From a therapeutic point of view also it is important as showing the advisability of excising the primary chancre in order to prevent its remaining as a focus of infection.

Following this paper is a note from Professor Hoffmann to the effect that he has often been able to demonstrate living spirochaetes in syphilitic scars.

H. D.

EXPERIMENTS WITH URTICA URENS. WINTERITZ. (*Archiv f. Derm. u. Syph.*, vol. lxxxviii, p. 299.)

THE active substance was by Dragendorff thought to be a mixture of free formic acid, an enzyme and a glucoside. Winteritz partly confirmed Perret's experiments in that he injected alcohol extracts of stinging nettles intra-venously into dogs, and found that itching and sneezing resulted, but no urticarial lesions. Previous heating of the mixture caused, as in Perret's experiments, considerable diminution in the symptoms.

Breathing and pulse were diminished in frequency, and blood-pressure fell on intravenous injection of active extract.

J. L. B.

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